General

Guideline Title

Sentinel lymph node biopsy and axillary node dissection in early stage breast cancer.

Bibliographic Source(s)

Alberta Provincial Breast Tumour Team. Sentinel lymph node biopsy and axillary node dissection in early stage breast cancer. Edmonton (Alberta): Alberta Health Services, Cancer Care; 2012 Aug. 16 p. (Clinical practice guideline; no. BR-004). [75 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

1. Axillary Staging. Sentinel lymph node biopsy (SLNB) is recommended for axillary staging of all patients with clinically node negative early-stage breast cancer. Patients with pre-operative biopsy proven nodal metastases should undergo axillary lymph node dissection (ALND) upfront.
2. Special Clinical Scenarios. Described below are three clinical situations: those in which there is a clear role for SLNB, those in which SLNB is not recommended, and those in which the role of SLNB is unclear (see also Table 1 in the original guideline document).
    - There is sufficient evidence to support the use of SLNB in patients with T1-2 tumours, multicentric tumours, ductal carcinoma in situ (DCIS) (with mastectomy), older age, obesity, and bilateral breast cancer. Clinicians and patients should note that older age and/or obesity are risk factors for failed SLN mapping.
    - SLNB is not recommended for patients with inflammatory T4 breast cancer, clinically positive nodes, or prior axillary surgery.
        - For clinically suspicious nodes, preoperative needle biopsy (fine needle aspiration [FNA] or core) can be performed; patients with a biopsy confirming metastatic disease should proceed directly to ALND.
    - The role of SLNB is less clear in the following circumstances: internal mammary lymph nodes, before preoperative systemic therapy, T3 or T4 tumours, DCIS (without mastectomy), suspicious palpable axillary nodes, after preoperative systemic therapy, prior diagnostic or excisional breast surgery, prior non-oncologic breast surgery, and pregnancy. For pregnant patients, there are concerns about the safety of blue dye; decisions should be made on a case by case basis.
3. Role of Additional Surgery. Described below are the circumstances in which ALND *is* recommended, circumstances in which ALND *may not* be recommended, and circumstances in which ALND is not recommended (see also Table 2 in the original guideline document).
    - ANLD is recommended in:
        - Patients with positive results from a pre-operative needle biopsy of clinically suspicious nodes.
        - All patients with positive findings on SLNB according to routine histopathologic examination

        - Data from a meta-analysis of 1842 patients demonstrates that among patients with a positive SLN, 48.3% were found to have additional node disease on ALND (Lyman et al., 2005; Kim, Giuliano, & Lyman, 2006).
        - Metastasis is found in nonsentinel nodes in approximately 10% of patients with isolated tumor cells in the SLN and in 20% to 35% of patients with micrometastases in the SLN (Lyman et al., 2005; McCready et al., 2004).
        - Patients in whom there was a failed attempt to localize a sentinel node.
    - ALND may not be recommended in:
        - Patients with life-shortening co-morbidities.
        - Patients with high perioperative risk.
        - Recent data from the Z0011 trial (2011) supports omission of ALND in a select group of patients with two or fewer positive nodes who are treated with breast conserving surgery (clinical T1-2 N0 M0 treated with whole breast irradiation and adjuvant systemic therapy) (Giuliano et al., 2011).
        - A decision to omit ALND should be made on a case by case basis with multidisciplinary input, ideally in a tumour board setting, if available.
    - ALND is not recommended: in patients with negative findings on SLNB.
    - Please refer to Appendix 1 for the Alberta Provincial Breast Tumour Team's consensus-based guidelines for multidisciplinary referral and discussion in node positive patients.
4. Technical Considerations. Sentinel lymph node mapping and localization has been shown to be highest using the periareolar dual injection technique with radioisotope and vital blue dye. Pathologic evaluation of excised sentinel lymph nodes should be evaluated with cut sections no thicker than 2.0 mm.
    - The identification of the SLNs should be guided by hand held gamma probe readings, allowing the surgeon to identify the sentinel node/s with the probe.
        - The 10% rule may be employed to identify SLNs (i.e., all nodes with a count greater than 10% of the hottest count is considered a SLN) as well as visual inspection for blue-stained nodes.
        - Removal of no more than four SLNs has been associated with low false negative rates; minimal additional information is provided from five or more nodes and the risk of additional morbidity is greater.
        - The surgeon should palpate for clinically suspicious nodes which are considered to be SLNs.
    - With the use of the radioisotope, it is also possible to demonstrate that radioactive nodes have been removed by performing ex vivo counts on the resected tissue.
    - The use of serial sections no thicker than 2.0 mm allows for the recognition of small metastatic deposits that might be missed by the examination of a lymph node that has been bivalved; hematoxylin & eosin staining is routinely employed. The use of immunohistochemistry (IHC) evaluation should not be used routinely (Giuliano et al., 2011; Krag et al., 2010).
5. Risks and Benefits of Sentinel Lymph Node Biopsy. The following risks and benefits have been associated with the use of SLNB:
    - SLNB is associated with reduced morbidity with equivalent positive node detection rates, compared with ALND, as it is a less invasive surgery (outpatient procedure and no need for drains), has fewer complications (e.g., sensory changes, lymphedema), and has enhanced pathologic staging.
    - Possible allergic reactions to blue dye represent a potential harm. Skin necrosis has been associated with methylene blue use.
    - Physicians should demonstrate caution regarding false-negative results; success of the procedure (i.e., low false-negative rates) is determined by several quality indicators, including team experience, case volume, and adherence to established protocols in nuclear medicine, pathology, and surgery.
6. Operational Considerations. SLNB should be performed by an experienced team to ensure that results are equivalent to those obtained with ALND.
    - The proportion of patients successfully mapped correlates with false-negative rates and is a reasonable indicator of quality; consistent pathology and nuclear medicine protocols need to be adhered to.
    - The recommended surgeon training includes completion of at least one of the following:
        - Training during a residency or fellowship program
        - Mentorship with an experienced surgeon (may include a formal didactic course)
        - Combining the procedure with a number of completion dissections to demonstrate acceptable accuracy (may include a formal didactic course)
    - The minimum system recommendations are that clinicians and patients should have access to:
        - A licensed nuclear medicine facility that follows a defined SLNB protocol to perform injection by nuclear medicine personnel or the surgeon
        - A surgeon with appropriate training and experience in sentinel node detection and extraction and access to a hand-held gamma probe, which is used to detect the SLN
        - A pathologist who assesses the SLN specimens according to a standardized protocol

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Early-stage breast cancer

Guideline Category

Evaluation

Management

Clinical Specialty

Family Practice

Nuclear Medicine

Obstetrics and Gynecology

Oncology

Pathology

Surgery

Intended Users

Clinical Laboratory Personnel

Physicians

Guideline Objective(s)

- To establish a standard of care in Alberta for patients with early-stage breast cancer, with respect to the management of the axillary nodes
- To address the indications for sentinel lymph node biopsy, management of patients with a positive finding, and considerations for implementing this procedure in an institution

Target Population

Patients with newly diagnosed, early-stage breast cancer

Interventions and Practices Considered

1. Sentinel lymph node biopsy (SLNB) for axillary staging
2. Axillary lymph node dissection
3. Technical considerations for sentinel lymph node mapping and localization
    - Periareolar dual injection technique with radioisotope and vital blue dye

    - Pathologic evaluation of excised sentinel lymph nodes
4. Operational considerations (use of trained, experienced surgical and pathology team)

Major Outcomes Considered

- Sentinel lymph node (SLN) detection rates
- Disease-free and overall survival rates
- Regional and axillary recurrence rates
- False-negative rates and complications associated with SLN biopsy (SLNB)

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Research Questions

Specific research questions to be addressed by the guideline document will be formulated by the guideline lead(s) and Knowledge Management (KM) Specialist using the PICO question format (patient or population, intervention, comparisons, outcomes).

Guideline Questions

1. Should sentinel lymph node biopsy (SLNB) be recommended as standard of care for patients with early-stage breast cancer?
2. What is the role of SLNB in special situations in clinical practice? (i.e., large and locally advanced invasive tumours, multicentric tumours, inflammatory breast cancer, ductal carcinoma in situ (DCIS), older age (65 years or more), obesity, male breast cancer, pregnancy, evaluation of the internal mammary nodes, presence of suspicious palpable axillary nodes, prior breast or axillary surgery, and preoperative systemic therapy?
3. Which patients should undergo axillary lymph node dissection (ALND)? Can ALND be avoided in patients with negative findings on SLNB? Is ALND necessary for all patients with positive findings on SLNB? Which patients should be referred for multidisciplinary referral and discussion?
4. What are the benefits and risks associated with SLNB? How can risks (i.e., complications and false-negative results) be minimized (e.g., surgeon experience, institution criteria, etc.)?
5. What are the recommended surgeon experience/training and organizational criteria and resources for performing SLNB?
6. How should SLNB be performed (i.e., what are the appropriate mapping technique, operative technique, and histological technique)?

Search Strategy

The MEDLINE, Cochrane, and CANCERLIT databases, as well as American Society of Clinical Oncology (ASCO) abstracts and proceedings were searched for literature relevant to these topics. The search included practice guidelines, systematic reviews, meta-analyses, randomized controlled trials, and clinical trials.

Literature published between 1950 and March 2011, comparing sentinel lymph node biopsy with axillary lymph node dissection, was collected using the following search terms: "sentinel lymph node biopsy" AND "lymph node dissection" OR "axillary node dissection" AND "breast cancer." Literature published between 1950 and March, 2011, pertaining to axillary lymph node dissection in sentinel node positive breast cancer patients, was collected using the following search terms: "lymphadenectomy" OR "sentinel lymph node biopsy" OR "axillary lymph node dissection" and "breast cancer."

A total of five practice guidelines and seven randomized controlled trials were identified. In addition, several other prospective cohort studies (e.g., non-controlled clinical trials) were also considered as evidence.

Following a review of several existing guidelines on this topic, the Alberta Provincial Breast Tumour Team's SLNB guideline working group agreed

to adapt the Cancer Care Ontario (CCO, 2009) guideline on SLNB in early-stage breast cancer. The CCO (2009) recommendations were updated for use in Alberta, following an update of the evidence on this topic, from the MEDLINE and EMBASE databases (May 2008 to March 2011).

Number of Source Documents

The recommendations were adapted from two existing guidelines; 75 documents were included in the review and formulation of the adapted recommendations.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Updated evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial Breast Tumour Team and a Knowledge Management (KM) Specialist from the Guideline Utilization Resource Unit (GURU). A detailed description of the methodology followed during the guideline development process can be found in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field).

Evidence Tables

Evidence tables containing the first author, year of publication, patient group/stage of disease, methodology, and main outcomes of interest are assembled using the studies identified in the literature search. Existing guidelines on the topic are assessed by the KM Specialist using portions of the Appraisal of Guidelines Research and Evaluation (AGREE) II instrument (http://www.agreetrust.org) and those meeting the minimum requirements are included in the evidence document. Due to limited resources, GURU does not regularly employ the use of multiple reviewers to rank the level of evidence; rather, the methodology portion of the evidence table contains the pertinent information required for the reader to judge for himself the quality of the studies.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Formulating Recommendations

The working group members formulated the guideline recommendations based on the evidence synthesized by the Knowledge Management (KM) Specialist during the planning process, blended with expert clinical interpretation of the evidence. As detailed in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field), the working group members may decide to adopt the recommendations of another institution without any revisions, adapt the recommendations of another institution or institutions to better

reflect local practices, or develop their own set of recommendations by adapting some, but not all, recommendations from different guidelines.

The degree to which a recommendation is based on expert opinion of the working group and/or the Provincial Tumour Team members is explicitly stated in the guideline recommendations. Similar to the American Society of Clinical Oncology (ASCO) methodology for formulating guideline recommendations, the Guideline Utilization Resource Unit (GURU) does not use formal rating schemes for describing the strength of the recommendations, but rather describes, in conventional and explicit language, the type and quality of the research and existing guidelines that were taken into consideration when formulating the recommendations.

Following a review of several existing guidelines on this topic, the Alberta Provincial Breast Tumour Team's sentinel lymph node biopsy (SLNB) guideline working group agreed to adapt the Cancer Care Ontario (CCO, 2009) guideline on SLNB in early-stage breast cancer. The CCO (2009) recommendations were updated for use in Alberta, following an update of the evidence on this topic, from the MEDLINE and EMBASE databases (May 2008 to March 2011).

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

This guideline was reviewed and endorsed by the Alberta Provincial Breast Tumour Team.

When the draft guideline document is completed, revised, and reviewed by the Knowledge Management Specialist and the working group members, it is sent to all members of the Provincial Tumour Team for review and comment. The working group members then make final revisions to the document based on the received feedback, as appropriate. Once the guideline is finalized, it is officially endorsed by the Provincial Tumour Team Lead and the Executive Director of Provincial Tumour Programs.

Evidence Supporting the Recommendations

References Supporting the Recommendations

Giuliano AE, Hunt KK, Ballman KV, Beitsch PD, Whitworth PW, Blumencranz PW, Leitch AM, Saha S, McCall LM, Morrow M. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: A randomized clinical trial. JAMA. 2011 Feb 9;305(6):569-75. [40 references] PubMed

Kim T, Giuliano AE, Lyman GH. Lymphatic mapping and sentinel lymph node biopsy in early-stage breast carcinoma: a metaanalysis. Cancer. 2006 Jan 1;106(1):4-16. [97 references] PubMed

Krag DN, Anderson SJ, Julian TB, Brown AM, Harlow SP, Costantino JP, Ashikaga T, Weaver DL, Mamounas EP, Jalovec LM, Frazier TG, Noyes RD, Robidoux A, Scarth HM, Wolmark N. Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial. Lancet Oncol. 2010 Oct;11(10):927-33. PubMed

Lyman GH, Giuliano AE, Somerfield MR, Benson AB 3rd, Bodurka DC, Burstein HJ, Cochran AJ, Cody HS 3rd, Edge SB, Galper S, Hayman JA, Kim TY, Perkins CL, Podoloff DA, Sivasubramaniam VH, Turner RR, Wahl R, Weaver DL, Wolff AC, Winer EP. American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. J Clin Oncol. 2005 Oct 20;23(30):7703-20. [147 references] PubMed

McCready DR, Yong WS, Ng AK, Miller N, Done S, Youngson B. Influence of the new AJCC breast cancer staging system on sentinel lymph node positivity and false-negative rates. J Natl Cancer Inst. 2004 Jun 2;96(11):873-5. PubMed

Type of Evidence Supporting the Recommendations

The recommendations were adapted from an existing guideline (see the "Adaptation" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of sentinel lymph node biopsy and axillary node dissection in early stage breast cancer

Potential Harms

- Axillary node dissection (ALND) is associated with significant morbidity, including arm lymphedema, pain, and decreased quality of life.
- Possible allergic reactions to blue dye represent a potential harm. Skin necrosis has been associated with methylene blue use.
- For pregnant patients, there exist concerns about the safety of blue dye. Several randomized controlled trials excluded pregnant patients. However, radiation exposure to the fetus using non-iodine radioisotopes in the dosages used for the sentinel node technique appear to be minimal. The Cancer Care Ontario (2009) guideline states that most members of their Expert Panel would use the sentinel lymph node biopsy (SLNB technique in a pregnant woman beyond the first trimester, weighing risk versus benefit on a case-by-case basis.
- Physicians should demonstrate caution regarding false-negative results of SLNB.

Contraindications

Contraindications

Sentinel lymph node biopsy (SLNB) is contraindicated for patients with clinically positive nodes, as it has been suggested that the path of the dye or the radio-colloid agent may be blocked from tumour cells infiltrating the lymph vessels, which could prevent the identification of the true sentinel node(s) and result in failure of the procedure or false negative results.

Qualifying Statements

Qualifying Statements

The recommendations contained in this guideline are a consensus of the Alberta Provincial Breast Tumour Team and represent a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

Implementation of the Guideline

Description of Implementation Strategy

- Present the guideline at the local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services Web site.
- Send an electronic notification of the new guideline to all members of Alberta Health Services, Cancer Care.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Alberta Provincial Breast Tumour Team. Sentinel lymph node biopsy and axillary node dissection in early stage breast cancer. Edmonton (Alberta): Alberta Health Services, Cancer Care; 2012 Aug. 16 p. (Clinical practice guideline; no. BR-004). [75 references]

Adaptation

The recommendations were adapted from the following guidelines:

- George R, Quan ML, McCready D, et al. and the Expert Panel on SLNB in Breast Cancer. Sentinel Lymph Node Biopsy in Early-stage Breast Cancer: Guideline Recommendations. A Quality Initiative of Cancer Care Ontario's Surgical Oncology Program (SOP) and Cancer Care Ontario's Program in Evidence-Based Care (PEBC). Report Date: July 14, 2009.
- Lyman GH, Guiliano AE, Somerfield MR, et al. American Society of Clinical Oncology Guideline Recommendations for Sentinel Lymph Node Biopsy in Early-Stage Breast Cancer. 2005. J Clin Onc 23(30):7703-21.

Date Released

2012 Aug

Guideline Developer(s)

CancerControl Alberta - State/Local Government Agency [Non-U.S.]

Source(s) of Funding

Alberta Health Services, Cancer Care

Guideline Committee

Alberta Provincial Breast Tumour Team and Provincial Gynecologic Oncology Team

Composition of Group That Authored the Guideline

Not stated

Financial Disclosures/Conflicts of Interest

Participation of members of the Alberta Provincial Breast Tumour Team and the Alberta Provincial Gynecologic Oncology Team in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. There was no direct industry involvement in the development or dissemination of this guideline. Alberta Health Services, Cancer Care recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. Some members of the Alberta Provincial Breast Tumour Team and Alberta Provincial Gynecologic Oncology Team are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Alberta Health Services Web site .

Availability of Companion Documents

The following is available:

- Guideline utilization resource unit handbook. Edmonton (Alberta): Alberta Health Services, Cancer Care; 2011 Dec. 5 p. Electronic copies: Available in Portable Document Format (PDF) from the Alberta Health Services Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on December 13, 2012. The information was verified by the guideline developer on February 1, 2013.

Copyright Statement

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